IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

In re Patent Application of

KOZLOV et al.

Serial No. 09/839,164

Filed: April 23, 2001

Title: INHIBITOR OF STEM CELL PROLIFERATION AND USES THEREOF

Atty Dkt. 1331-338
C# M#

TC/A.U.: 1653

Examiner: K.C. Carlson

Date: April 15, 2004

Image AU 1653

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

☐ **Correspondence Address Indication Form Attached.**

☐	**NOTICE OF APPEAL** Applicant hereby **appeals** to the Board of Patent Appeals and Interferences from the last decision of the Examiner. ($ 330.00)	$	
☒	An appeal **BRIEF** is attached in triplicate in the pending appeal of the above-identified application ($ 330.00)	$	330.00
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☐	A reply brief is attached in triplicate under Rule 193(b)		**(no fee)**
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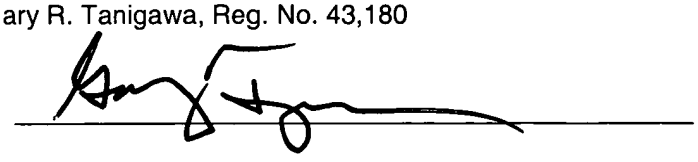
Signature: 

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of
KOZLOV et al.
Appln. No. 09/839,164
Filed: April 23, 2001
FOR: INHIBITOR OF STEM CELL PROLIFERATION AND USES THEREOF

Confirmation No.: 6786
Atty. Ref.: 1331-338
T.C. / Art Unit: 1653
Examiner: K.C. Carlson

* * *

BRIEF UNDER 37 CFR § 1.191 ET SEQ.

April 15, 2004

MS Appeal Brief – Patents
U.S. Patent and Trademark Office
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants submit this Brief under 37 CFR § 1.192 et seq. (in triplicate) to appeal the Examiner's final rejections of claims 30-32 as set forth in her Office Action (Paper No. 12) mailed June 3, 2003. A Notice of Appeal was timely filed on December 3, 2003.

Reversal of the Examiner's claim rejections by the Board of Patent Appeals and Interferences (the "Board") is respectfully requested.

(1) REAL PARTY IN INTEREST

The assignee, Wellstat Therapeutics Corporation, holds all rights in the subject invention by virtue of (a) an assignment recorded on January 3, 1995 at reel 7341 and frame 0661 and (b) a change of name recorded on April 2, 2004 at reel 14489 and frame 616 in the U.S. Patent and Trademark Office.

(2) RELATED APPEALS AND INTERFERENCES

Appellants, the assignee, and its legal representative are unaware of any related appeal or interference which will directly affect, be directly affected by, or have a bearing on the Board's decision in this appeal.

(3) STATUS OF CLAIMS

Claims 30-32 were examined in this application and are at issue in this appeal. The claims on appeal are set forth in the Appendix. Claims 1-29 were canceled without prejudice or disclaimer.

(4) STATUS OF AMENDMENTS

No amendment was filed subsequent to final rejection.

(5) SUMMARY OF INVENTION

The invention involved in this appeal is directed to a pharmaceutical composition consisting essentially of alpha globin of hemoglobin in a pharmaceutically acceptable carrier (claim 30), consisting essentially of beta globin of hemoglobin in a pharmaceutically acceptable carrier (claim 31), or consisting of both alpha globin and beta globin of hemoglobin in a pharmaceutically acceptable carrier (claim 32). Original claims 1-5 and the specification (e.g., page 13, lines 14-19; page 18, lines 23-27) support the pending claims.

Therefore, the invention as presently claimed is clearly supported by the original disclosure filed by Appellants.

(6) ISSUES

A. Under 35 U.S.C. 112, 2nd paragraph, was it proper to reject claims 30-32 as allegedly "vague and indefinite"?

B. Under 35 U.S.C. 102(b), was it proper to reject claims 30-32 as allegedly anticipated by Tame et al. (J. Mol. Biol. 218:761-767, 1991)?

C. Under 35 U.S.C. 102(e), was it proper to reject claims 30-32 as allegedly unpatentable over Hoffman et al. (U.S. Patent 5,449,759)?

(7) GROUPING OF CLAIMS

Claims 30-32 stand or fall together.

(8) ARGUMENTS

A. Mass is a Clear and Definite Claim Limitation Without Recitation of Concentration

Claims 30-32 were rejected under Section 112, second paragraph, as allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." The Examiner explained on page 2 of Paper No. 12 that "it is not clear what present in the milligram amounts means, as a composition comprises a concentration of a particular item, such as grams/liter, for example." Appellants traverse.

"If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more." *Miles Laboratories, Inc. v. Shandon Inc.*, 997 F.2d 870, 875, 27 USPQ2d 1123, 1126 (Fed. Cir. 1993), *citing Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1375, 231 USPQ 81, 87 (Fed. Cir. 1986). The rejected claims are directed to a pharmaceutical composition in which from 0.1 mg to 6 g of alpha and/or beta globin is present regardless of its concentration in the composition. There is no ambiguity as to whether a given composition is included or excluded from the claim and no reason has been given as to why the person of skill in the art would not understand the scope of the claim. Appellants' claims define the amount of active ingredient in their invention by mass.

The Examiner asserts that it is "standard chemical and pharmaceutical practice" to recite concentration in describing the contents of a composition. Page 2 of Paper No. 12. Appellants are unaware of such a "standard" where pharmaceutical compositions are described by concentration instead of mass. And no evidence or legal authority has been cited by the Examiner to support her assertion. In the absence of such support, this rejection under Section 112, second paragraph, should be reversed.

Furthermore, there is no reason for requiring concentration rather than mass to describe a pharmaceutical composition. Appellants are unaware of such a "standard" requiring pharmaceutical compositions to be described by concentration and forbidding them to be described by mass. It is equivalent to describe the amount of alpha and/or

beta globin in pharmaceutical compositions by concentration or mass because such quantities can be converted from one to the other. Here, Appellants have described their invention by the mass of alpha and/or beta globin in the pharmaceutical composition (see page 14, line 7, of the specification).

Appellants request that the Board reverse the Examiner's rejection under Section 112, second paragraph, because the pending claims are clear and definite.

B/C. Prior Art Does Not Teach 0.1 mg to 6 g of Alpha and/or Beta Globin

Claims 30-32 were rejected under Section 102(b) as allegedly anticipated by Tame et al. (J. Mol. Biol. 218:761-767, 1991) and under Section 102(e) as allegedly anticipated by Hoffman et al. (U.S. Patent 5,449,759). Appellants traverse.

To be anticipated under Section 102, each and every element of a claim must be disclosed, either explicitly or inherently, in a single reference. *Lewmar Marine, Inc., v. Barient, Inc.*, 827 F.2d 744, 747, 3 USPQ2d 1766, 1767 (Fed. Cir. 1987). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." *Continental Can Co. v. Monsanto Co.*, 948 F.2d 1264, 1269, 20 USPQ2d 1746, 1749 (Fed. Cir. 1991) *quoting In re Oelrich*, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981). The extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1951 (Fed. Cir. 1999) *quoting Continental Can id.* at 1268, 20 USPQ2d at 1749.

The Examiner states on page 3 of Paper No. 12, "Claims 30 to 32 are anticipated because there is no concentration provided in the claims, and enough of the solutions taught in Tame et al. can be made to comprise 0.1 mg to 6 g of globin." But this is insufficient basis to make a Section 102 rejection because the issue in anticipation is not what can be made, but what was made or disclosed. Tame et al. do not disclose the making of a solution containing from 0.1 mg to 6 g of alpha globin and/or beta globin. Here, the volume of the solution made by Tame et al. is not disclosed; only the concen-

tration of the solution (5 mg/ml or 0.25 mg/ml) is taught. Therefore, lacking a disclosure of the solution's volume, Tame et al. do not disclose the range of masses recited in claims 30-32 and the cited reference does not anticipate the claimed invention. An anticipation rejection cannot be based on probabilities or possibilities because the allegedly inherent limitation must be disclosed in the prior art reference. *Robertson.*

As in Tame et al. discussed above, it is undisputed that Hoffman et al. do not disclose a composition containing the recited amount of any globin chain. Instead, the rejection is impermissibly based on what could be made. Thus, the Examiner states on page 5 of Paper No. 12, "Just the single millimeter of Hoffman et al.'s solution meets the claim amount recitation." But Hoffman et al. do not teach or suggest a solution which is only one millimeter in volume. Instead, it was alleged by the Examiner that solutions containing alpha or beta globin at the concentrations disclosed by Hoffman et al. may be made at whatever volume is needed to anticipate the claims. This an impermissible basis for a Section 102 rejection as noted above (see *Robertson*). Therefore, Hoffman et al. do not disclose each and every element of claims 30-32.

A prior art reference does not anticipate a claim without actually or inherently teaching all of the claim limitations. *Lewmar Marine.* Here, the solutions of Tame et al. and Hoffmann et al. must have a volume and contain a certain mass of alpha or beta globin. But no evidence has been presented by the Examiner to show that the mass of alpha or beta globin in the solutions of the cited references would necessarily satisfy the requirements of the claims and, thus, attempt to shift the burden to Appellants to prove otherwise. The mass of alpha or beta chain in their solutions is an inherent property of the solution, but it is not a quantity which can be manipulated at will by the Examiner to produce the limitations of the claims.

It was twice alleged by the Examiner on pages 4 and 5 of Paper No. 12, "This jug/beaker/vial/syringe of solution must have the alpha globin chain present in 0.1 mg to 6 g" (emphasis added) in reference to the disclosures of Tame et al. and Hoffman et al. As noted above, there was no indication in the cited references of the volumes of their solutions so allegations that a "single milliliter of [the cited reference's] solution[s] meets

the claim amount recitation" (pages 4 and 5 of Paper No. 12) are mere speculations by the Examiner and not supported by the evidence.

It was further alleged by the Examiner on pages 4 and 5 of Paper No. 12, "The composition must be suitable for subcutaneous administration, meaning it can be administered s.c." (emphasis added). But the human alpha globin chain was produced in *E. coli* in both cited references and purification of the apoproteins prior to inclusion of heme did not remove endotoxin which one of ordinary skill in the art would expect to be in the solutions of the cited references. Without such removal of a substance known to be dangerous to humans, the solutions of the cited references are not suitable for subcutaneous administration. The unsubstantiated allegations of the Examiner do not make up for this lack of evidence.

Best and *Gray* cited by the Examiner on page 5 of Paper No. 12 are not relevant to this situation. In *Gray*, it was held that since the issue was "whether the prior art [human nerve growth] factor is identical or patentably distinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved." *Ex parte Gray*, 10 USPQ2d 1922, 1925. But the issue here is not whether the globin chains required by claims 30-32 are identical to the alpha or beta globin of the cited references. Here, the active ingredients of the claimed pharmaceutical composition are identical to the isolated, native globin chains without heme. Furthermore, Appellants here have not discovered an inherent biological activity or function for the composition which was not described in the cited references. Cf. *In re Best*, 195 USPQ 430, 432-3. Instead, the mass of alpha and/or beta globin is a physical quantity and a limitation explicitly recited in claims 30-32, unlike the functional limitations considered in *Best* and other cases dealing with inherency. The Examiner has not provided sufficient grounds to shift the burden to Appellants because there was no evidence presented in the Office Action to indicate that the solutions described in the cited references were necessarily made in volumes which would result in the "identical or substantially identical" mass of alpha and/or beta globin recited in the pending claims. Appellants have requested that the Examiner cite the evidence which supports her allegation that the solutions of Tame et

al. and Hoffman et al. were made in amounts within the range recited in the claims, but no evidence was cited in response.

The Manual of Patent Examining Procedure discusses the circumstances under which the prior art may anticipate a composition claim which recites a range such as 0.1 mg to 6 g. M.P.E.P. § 2131.03 ("In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with 'sufficient specificity to constitute an anticipation under the statute"). Here, Tame et al. and Hoffman et al. are silent on the mass of globin chain in their compositions. The references' disclosure of a concentration and the assertion by the Examiner that "enough of the solutions . . . can be made" does not provide sufficient specificity to anticipate the range of masses which is recited in the pending claims.

In the absence of acceptable evidence that the prior art disclosed pharmaceutical compositions with alpha and/or beta globin in an amount of 0.1 mg to 6 g as an inherent characteristic, the burden does not shift to Appellants to prove otherwise.

Appellants request that the Board reverse the Examiner's Section 102 rejections because the cited references fail to disclose all limitations of the claimed invention.

For the reasons discussed above, Appellants respectfully request that the claim rejections should be reversed by the Board. Appellants submit that the pending claims are in condition for allowance and earnestly request an early Notice to that effect.

Respectfully submitted,

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(9) APPENDIX

30. A pharmaceutical composition consisting essentially of the alpha globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and said alpha globin chain is present in an amount of 0.1 mg to 6 g.

31. A pharmaceutical composition consisting essentially of the beta globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and said beta globin chain is present in an amount of 0.1 mg to 6 g.

32. A pharmaceutical composition consisting of the alpha globin chain of hemoglobin and the beta globin chain of hemoglobin in a pharmaceutically acceptable carrier, wherein the composition is suitable for subcutaneous administration and said beta globin chain and said alpha globin chain are each present in an amount of 0.1 mg to 6 g.